Case Report:
Gaucher's Disease

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Gaucher's disease is the commonest lysosomal storage disorder. It is a rare disorder inherited as an autosomal recessive trait, caused by mutation of the glucocerebrosidase gene. The adult type of the disease is the commonest type; the infantile and juvenile type being very rare. We received two cases of Gaucher's disease (one infant and one child) at the Pathology Department of Allama Iqbal Medical College, Lahore, from the Pediatric Department of Jinnah Hospital, Lahore. Both patients presented with massive hepatosplenomegaly. Routine blood examination and bone marrow aspiration was carried out. Bone marrow smears showed Gaucher cells. Liver biopsy also showed Gaucher cells. Periodic acid Schiff (PAS) stain on bone marrow smears and liver biopsy revealed Gaucher cells to be positive for PAS.

Key words: PAS(Period acid Schiff), Hb(Haemoglobin)

Gaucher's disease is the most common lipid storage disorder. It is caused by the genetic deficiency of an enzyme á-glucocerebrosidase[1-5]. Due to deficiency of the enzyme, hydrolysis of glucocerebroside to glucose and ceramide is impaired. Glucocerebroside is formed continually from the catabolism of glycolipids, derived mainly from the cell membranes of dying red cells and leucocytes[6]. As a result insoluble glucose-ceramide accumulates mainly within reticuloendothelial cells of the body. In some types glucocerebroside accumulates in the central nervous system as well[3,6].

Gaucher's disease is inherited as an autosomal recessive trait. The gene is located on chromosome 1 q 21. The disease is usually caused by gene mutation, deletion or fusion[2,7]. At least 36 different gene mutations have been identified, but four are more common[2,8].

Clinically three types of Gaucher's disease are seen; type 1, type 2 and type 3. Type 1 is the adult or non-neuronopathic type, whereas type 2 and 3 are the infantile and juvenile type which have central nervous system involvement[1-2,5,7]. Type 1 is the commonest form, seen in about 99% of cases, and is most prevalent in Ashkanazi Jews[1-2,5].

Diagnosis of Gaucher's disease is made by the identification of the distinctive storage cell in the bone marrow aspirate and/or liver and spleen biopsy[1,6,9]. Confirmation of the diagnosis is by the enzyme assay of á-glucocerebrosidase, which will be deficient[1-3,9-11].

In the past, Gaucher's disease has been treated symptomatically, i.e. partial or total splenectomy being carried out for thrombocytopenia.[2]. However, since 1974, enzyme replacement therapy is done[2-3,7,10,12]. Recombinant enzyme preparation became available in 1994[3-11]. Gene therapy and bone marrow transplant are still more recent forms of treatment[11].

Case Report

Case 1

Faiza, 1 year old girl presented with fever and cough for the last 20 days. She had delayed milestones and was unable to sit on her own. She had a history of progressive abdominal distension for the last six months. On examination she was pale and had massive hepatosplenomegaly.

Blood picture showed haemoglobin of 8.5 Gm/dl, total leucocyte count was 6.9x109/L and platelets were 120x109/L. Differential leucocyte count showed neutrophils 34%, lymphocyte 63%, monocytes 2%, eosinophils 1%. Red blood cell morphology showed moderate hypochromia, anisopoikilocytosis with macrocytosis and microcytosis.

Bone marrow examination revealed moderately cellular smears and fragments with moderately cellular erythropoiesis, myelopoiesis and megakaryopoiesis. There was infiltration by large cells which had rounded nuclei and abundant bluish-gray agranular cytoplasm giving a crumpled appearance. These large cells were positive for PAS staining. Diagnosis of Gaucher's disease was made.

Case 2

Rabia, a 5 years old girl, presented with progressive abdominal distension with abdominal mass since the age of 6 months. There was massive hepatosplenogegaly, on examination, liver was 12 cm palpable and spleen was 8 cm. There was no sign of chronic liver disease, ascites or portal hypertension. She also had intermittent fever for the last 4« years. Fever was high grade and was relieved by medicines. There was history of intermittent diarrhoea as well for the same duration; frequency of stools was 4-5/day and consistency was loose to semi-solid, of normal colour.

Blood picture revealed haemoglobin of 10 Gm/dl; total leucocyte cell was 7.9x109/L; platelets were 250x109/L; differential leucocyte count showed neutrophils 26%, lymphocytes 70%, monocytes 3% and eosinophils 1%. Red blood cell morphology was normocytic normochromic. Erythrocyte sedimentation rate was 120 nm fall at the end of the first hour. Liver function tests were normal. Ultrasound revealed massive hepatosplenomegaly with no focal mass and normal architecture and portal vein.

Bone marrow examination revealed good to hypercellular smears with active erythropoiesis and myelopoiesis; megakaryocytes were normal; mature lymphocytes were prominent. There was infiltration by large cells with small rounded nucleus; cytoplasm was abundant, bluish-gray in colour, agranular and giving a wrinkled appearance. These cells were PAS positive. Liver biopsy was done which showed a normal parenchyma of liver with scattered foci of aggregates of Gaucher cells which were large rounded to polygonal cells with central small nucleus and a fibrillar cytoplasm. PAS staining was done, Gaucher cells were positively stained. Diagnosis of Gaucher's disease was confirmed.

Discussion

Gaucher's disease is a rare genetic disease inherited as an autosomal recessive trait. Clinically three types of the disease are seen. Type II and type III disease collectively make up only about 1% of the cases diagnosed[2,6]. Two cases with Gaucher's disease are reported, one with type II disease and the other with type III disease.

Beutler[2] and Matalon[9] reported that type II or infantile type of Gaucher's disease starts at about 6 months of age presenting with splenomegaly, strabismus, trismus and dorsiflexion of head. Our patient presented with hepatosplenomegaly, strabismus and delayed milestones. She also had anaemia and thrombocytopenia at the time of presentation. Beutler2 has reported Thrombobocytopenia as a presenting feature; whereas Cotran et al6, Hoffbrand and Pettit7 and Matalon9 have mentioned pancytopenia.

Juvenile Gaucher disease presents at the age of 2-6 years with hepatosplenomegaly, hypersplenism and bone involvement. Neurological symptoms start in the 1st or even 2nd decade of life, as noted by Hoffbrand and Pettit[7], and Cotran et al[6]. Our patient presented at the age of 5 years with massive hepatosplenomegaly, repeated diarrhea and fever. Her complaints started within the first year of life. There were no neurological symptoms at the time of presentation. Her blood examination revealed normal counts and her liver function tests were also normal. Beutler[2] has reported thrombocytopenia due to splenomegaly; and abnormal liver function tests. Cotran et al[6] and Matalon[9] have reported pancytopenia as a result of hypersplenism.

Bone marrow examination was performed in both patients which showed infiltration by large cells with abundant bluish-gray, agranular, wrinkled cytoplasm and single rounded nuclei - Gaucher cells. These cells were PAS positive. Diagnosis of Gaucher's disease was made by the identification of such cells in the bone marrow as mentioned by Cotran et al[6], Beaudet[1] and Matalon[9]. Liver biopsy was performed in one patient which also showed infiltration by Gaucher cells which were positively stained by PAS stain. Cotran et al[6] also found infiltration of the liver by Gaucher cells which were positive for PAS stain.

The parents of both our patients were first cousins but there was no family history of Gaucher's disease. However, Shahinfar and Wenger[13] have reported the disease in a mother and son.

Conclusion

Diagnosis of Gaucher disease can be made by the identification of typical Gaucher cells in bone marrow aspirate or liver/spleen biopsy. Confirmation is by enzyme assay of glucocerebrosidase, but this facility is not readily available. Specific treatment is available in the form of commercially prepared enzyme, but the treatment is very expensive. Response to treatment is better in the adult type. So the prognosis in children is still rather bleak.

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